Accumulation of the gases produced during the fermentation of FODMAPs is likely one of the leading factors associated with symptom generation in IBS. The observed differences in timing and quantity of breath hydrogen illustrates the complexity of human and bacterial metabolism of the FODMAP substrates. Measuring breath hydrogen subsequent to the ingestion of a fixed FODMAP dose, provides a quantifiable indicator of the volume of colonic gas that would be produced under dietary conditions.

**References**
Introduction Refractory gastrointestinal symptoms are an increasingly recognised area of unmet need, which cause significant morbidity and impair the quality-of-life of patients with Cystic Fibrosis (CF). Recent studies have suggested a high prevalence of both gastro-oesophageal reflux and bowel symptoms in CF. However the association between reflux symptoms, oesophageal pH metrics, and overlapping bowel symptoms has not been studied.

Methods CF patients recruited from a tertiary clinic completed validated patient reported outcome measures for reflux (RESQ-7) and functional bowel symptoms (IBS-SSS), after undergoing 24-hour oesophageal pH and impedance studies. Subjects remained on their regular prescribed acid suppression for 6 weeks after using ABFES which was maintained over a 24-week period. High compliance with the treatment over the time period suggests acceptability. The findings are consistent with previous studies and suggest a fully powered controlled trial is required.

Results CF patients (n=40, median age 30 (range 18–48), 28 males, FEV1 50%, BMI 22 kg/m²), participated in the study. The majority of participants had reflux symptoms (31/40, 78%), and remained on acid suppression during the 24-hour oesophageal pH/impedance study. Overall, group median oesophageal acid exposure time (oesophageal pH<4 - 2.9%, IQR 7.9%), and Demeester scores (11.17, IQR 28.30), were within the normal range, suggesting adequate acid suppression. Strong correlations were seen between total IBS-SSS scores and reflux symptom scores (heartburn severity r_s=0.678, p<0.001 and frequency r_s=0.649, p<0.001, regurgitation severity (r_s=0.638, p<0.001) and frequency (r_s=0.627, p<0.001). By contrast, no correlation was seen between oesophageal pH-impedence metrics, with either reflux symptom scores (p=NS) or IBS-SSS scores (p=NS).

Conclusions This study is the first to demonstrate overlapping foregut and hindgut functional gastrointestinal symptoms in patients with CF using validated patient recorded outcome measures and objective reflux metrics. The correlation between reflux and bowel symptoms, independent of reflux measures, is intriguing, and suggests a possible mechanism of visceral hypersensitivity. The use of gut-brain neuromodulators in this difficult to treat group of patients may therefore have a role and warrants proper investigation.

Conclusions The study found a significant and clinically meaningful reduction in self-reported constipation symptoms for PwMS after six weeks of using ABFES which was maintained over a 24-week period. High compliance with the treatment over the time period suggests acceptability. The findings are consistent with previous studies and suggest a fully powered controlled trial is required.

PPI REFRACTORY 'REFLUX' SYMPTOMS ARE ASSOCIATED WITH BOWEL SYMPTOM SEVERITY IN PATIENTS WITH CYSTIC FIBROSIS

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Introduction Primary bile acid diarrhoea (BAD), also known as idiopathic bile acid malabsorption, is a common cause of chronic functional diarrhoea and irritable bowel syndrome with diarrhoea. BAD has been shown to be associated with fatty liver disease including non-alcoholic steatohepatitis (NASH), with shared mechanisms being reported. In our previous proof-of-concept study, patients with BAD had significant clinical improvements in stool type and frequency when treated for two weeks with the first-in-class farnesoid X receptor (FXR) agonist obeticholic acid (OCA). In a case report using OCA for 6 months, in addition to clinical improvement, normalisation of the diagnostic SeHCAT test was found. The aim of this study was to see if further evidence for benefits of FXR agonists on diarrhoea could be found in the recently published results from the 18-month interim analysis of a large phase 3 study of OCA in NASH (Younossi ZM, et al. Lancet 2019; 394:2184-2196). The published results of the interim analysis were analysed independently. Patients with NASH fibrosis (n=1968) had been randomly allocated to placebo, OCA 10 mg, or OCA 25 mg daily. Patient-reported adverse reactions had been recorded per protocol. Figures for newly incident events of diarrhoea and constipation were given. The frequencies of these events were compared between the groups.

Results Incidents of diarrhoea were reported in 12% of patients in the placebo-treated group. These were significantly fewer in both OCA-treatment groups, at 7% (p<0.005, Fischer’s exact tests). Incidents of constipation were the opposite, occurring in 5% with placebo treatment, 10% with OCA 10 mg and 11% with OCA 25 mg (p<0.003).

Conclusion Analysis of this trial of OCA in NASH patients indicates that treatment with FXR agonists reduces episodes of diarrhoea and increases constipation. This is presumably by the demonstrated effects of FXR agonists, stimulating FGF19 and reducing bile acid synthesis. Although the primary focus of the trial is on liver fibrosis, these results provide further evidence that FXR agonists can be a therapeutic option in BAD. Trials of FXR agonists in development should include analysis of effects on bowel function, and specifically look at the response in patients with BAD.